REMARKS

Reconsideration is requested.

Claims 1-32 are pending. Claims 29-32 have been added. Support for the new claims may be found throughout the specification. No new matter has been added.

The Examiner is requested, for completeness and clarity for the printer, to return an initialed and dated PTO 1449 Form which completely lists, including the country (EP) and date (12/1998), of the EP0882799A1 reference listed by the Examiner in the PTO 1449 Form returned with the Office Action of December 17, 2003.

The Examiner is further requested to completely indicate in the next Communication that a certified copy of the priority document has been received.

The Section 112, second paragraph, rejection of claims 23-28 is obviated by the above amendment of claim 22. Withdrawal of the rejection is requested.

The Section 112, first paragraph "enablement", rejection of claims 22-28 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following remarks and the attached Declaration.

The attached Declaration presents experimental data demonstrating ADCC activity of the recombinant antibody KM2550 (anti-Flt-1 human chimeric antibody) which can be used in the treatment method of the present invention. As shown in the experimental data, the recombinant antibody KM2550 has ADCC activity against leukemia cell line HSB-2 and leukemia cell line Jurkat in which the expression of Flt-1 was confirmed in the present specification.

Furthermore, the attached Steplewski et al (Proc. Natl. Acad. Sci. USA, 85, 4852-4856 (1988)) which is listed on the attached PTO 1449 Form[1]), is believed to describe a mouse IgG2a antibody CO17-1A having antitumor activity against colorectal cancer and human IgG1, IgG2, IgG3 and IgG4 chimeric antibodies of the CO17-1A. The ADCC activity of each antibody using various effector cells and the antitumor activity using a nude mouse are believed to be described. According to Fig. 7, when murine macrophages were used as effector cells, human IgG1 and human IgG4 chimeric antibodies exerted high ADCC activity. Fig. 8 shows the correlation between the degree of the ADCC activity and the in vivo antitumor activity. Accordingly, it is apparent that the antibody having ADCC activity has also in vivo antitumor activity.

The Examiner's concerns regarding cell-cell interactions of *in vivo* pathological states is, with due respect, not believed to be a concern with the presently claimed method as the presently claimed invention relates to a method for treating diseases caused by the tumorigenic change of a hematopoietic cell, which will be recognized by one of ordinary skill in the art as being immersed in the blood, and that the tumorigenic hematopoietic cells to be injured/targeted by the antibody of the present invention are similarly immersed in the blood. Accordingly, the antibody used in the treatment method of the presently claimed invention would not be influenced by the cell-cell interactions in both in vitro and in vivo conditions, which are the apparent concern of the Examiner. See, pages 4-5 of the Office Action dated December 17, 2003.

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[1] Return of an initialed copy of the attached PTO 1449 Form is requested, pursuant to MPEP § 609. Payment of the Rule 17(p) fee for consideration of the attached evidence is not believed to be required however the Office is authorized by the attached cover sheet to charge the undersigned's Deposit Account No. 14-1140 for any missing or deficient fee which the Office believes is required, such

Moreover, the applicants submit that the Examiner's "enablement" rejection of claims 22-24 is inconsistent with the Examiner's Section 102 rejection of claims 22-24 over Shitara (U.S. Patent No. 6,617,160) as if the cited art does in fact place the presently claimed invention in the art, as the Examiner asserts in the Section 102 rejections of claims 22-24, then one of ordinary skill is presumably also taught how to make and use the claimed invention. Elan Pharmaceuticals Inc. v. Mayo Foundation for Medical Education and Research, 68 USPQ2d 1373, 1375 (CA FC 2003) ("To serve as an anticipating reference, the reference must enable that which it is asserted to anticipate. 'A claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled.' " *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354, 65 USPQ2d 1385, 1416 (Fed. Cir. 2003). *See Bristol-Myers Squibb v. Ben Venue Laboratories, Inc.*, 246 F.3d 1368, 1374, 58 USPQ2d 1508, 1512 (Fed. Cir. 2001) ("To anticipate the reference must also enable one of skill in the art to make and use the claimed invention."); *PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1566, 37 USPQ2d 1618, 1624 (Fed. Cir. 1996) ("To anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter.")).

The claims are submitted to be supported by an enabling disclosure and withdrawal of the Section 112, first paragraph, rejection of claims 22-28 is requested.

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as for consideration of the attached evidence. Return of an initialed PTO 1449 Form, pursuant to MPEP § 609, is requested.

The provisional obviousness-type double patenting rejection of claims 22-28 over claims 1, 6, 7, 10, 34 and 49-50 of application Serial No. 10/160,232 and claims 3-5 and 9 of application Serial No. 10/009,723, is traversed. Withdrawal of the provisional rejection is requested as the Examiner's reliance on Serial No. 10/009,723, which was filed after the present application, is believed to be inappropriate. At a minimum, the Examiner is requested to hold the provisional rejection in abeyance until such time as allowable subject matter is identified.

The Section 102 rejection of claims 22-24 over Shitara is traversed. Reconsideration and withdrawal of the rejection are requested.

As noted above, the Examiner's Section 102 and Section 112 "enablement" rejections are believe to be inconsistent.

Moreover, The Examiner appears to assert that Shitara et al teach a method of treating a disease through the administration of an anti-human VEGF receptor flt-1 antibody, wherein the antibody can be monoclonal (col. 4, lines 46-50), wherein the monoclonal antibody is KM1732 (col., 4, lines 19-20), and that the administration of the anti-human VEGF receptor flt-1 antibody as taught by Shitara et al would also inherently treat diseases associated with tumorigenic changes of hematopoietic cells.

However, Shitara et al disclose at col. 15, liens 3-11 that the monoclonal antibodies of the present invention are useful for the immunological detection of human angiogenesis regions by immunocyte staining and for the diagnosis or treatment, through the inhibition of the biological activities of human VEGF, or diseases in which their morbid states progress by abnormal angiogenesis, such as proliferation or metastasis of solid tumors, arthritis in rheumatoid arthritis, diabetic retinopathy,

retinopathy of prematurity, psoriasis, and the like. That is, Shitara et al is believed to relate to a method for treating diseases in which their morbid states progress by abnormal angiogenesis.

The present invention relates however to a method for treating diseases caused by the tumorigenic change of a hematopoietic cell, and the method of the present invention is therefore distinguished from that of Shitara et al.

The claims are submitted to be patentable over Shitara and withdrawal of the Section 102 rejection of claims 22-24 is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____
B. J. Sadoff
Reg. No. 36,663

BJS:
1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100